

IN THE SPECIFICATION

Please replace paragraph [0006] with the following paragraph:

[0006] Accordingly, in one aspect, the invention features a nucleic acid molecule which encodes a 93870 protein or polypeptide, e.g., a biologically active portion of the 93870 protein. In a preferred embodiment, the isolated nucleic acid molecule encodes a polypeptide having the amino acid sequence of SEQ ID NO:2. In other embodiments, the invention provides an isolated 93870 nucleic acid molecule having the nucleotide sequence shown in SEQ ID NO:1[,], or SEQ ID NO:3, and the sequence of the DNA insert of the plasmid deposited with ATCC on ____ as Accession Number ____ (hereafter, "the deposited nucleotide sequence").

Please replace paragraph [0012] with the following paragraph:

[0012] In other embodiments, the invention provides 93870 polypeptides, e.g., a 93870 polypeptide having the amino acid sequence shown in SEQ ID NO:2 or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC Accession Number ____; an amino acid sequence that is sufficiently or substantially identical to the amino acid sequence shown in SEQ ID NO:2 or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC Accession Number ____; or an amino acid sequence encoded by a nucleic acid molecule having a nucleotide sequence which hybridizes under stringent hybridization conditions to a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3 or the nucleotide sequence of the insert of the plasmid deposited with ATCC Accession Number ____, wherein the nucleic acid encodes a full length 93870 protein or an active fragment thereof.

Please delete paragraph [0023].

Please replace paragraphs [0066]-[0067] with the following paragraphs:

[0066] A "non-essential" amino acid residue is a residue that can be altered from the wild-type sequence of 93870 (e.g., the sequence of SEQ ID NO:1 or 3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number ____) without abolishing or more preferably, without substantially altering a biological activity, whereas an "essential" amino acid residue results in such a change. For example, amino acid residues that are

conserved among the polypeptides of the present invention, e.g., those present in the seven transmembrane receptor domains, are predicted to be particularly unamenable to alteration.

[0067] A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (e.g., alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine). Thus, a predicted nonessential amino acid residue in a 93870 protein is preferably replaced with another amino acid residue from the same side chain family. Alternatively, in another embodiment, mutations can be introduced randomly along all or part of a 93870 coding sequence, such as by saturation mutagenesis, and the resultant mutants can be screened for 93870 biological activity to identify mutants that retain activity. Following mutagenesis of SEQ ID NO:1 or SEQ ID NO:3, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, the encoded protein can be expressed recombinantly and the activity of the protein can be determined.

Please replace paragraph [0025] with the following paragraph:

[0025] The G-protein coupled receptor family of seven transmembrane proteins is an extensive group of proteins, which transduce extracellular signals triggered by, e.g., hormones, neurotransmitters, odorants and light, by interaction with guanine nucleotide-binding (G) proteins. The N-terminus of G-protein coupled receptors is typically located on the extracellular side of the membrane and is often glycosylated, while the C-terminus is cytoplasmic and generally phosphorylated. G-protein coupled receptors typically have seven hydrophobic membrane spanning regions. Three extracellular loops alternate with three intracellular loops to link the seven transmembrane regions. Some G-protein coupled receptors possess a signal peptide. Generally, the most conserved portions of G-protein coupled receptors are the transmembrane regions and the first two cytoplasmic loops. A conserved arginine-aromatic doublet is present in the N-terminal extremity of the second cytoplasmic loop and may be implicated in the interaction with G proteins. Alignments of the domains of 1308 representative

GPCRs can be found at the ProDom release 2000.1 information from to Institut National de la Recherche Agronomique (INRA)/ Central National de la Recherche Scientifique (CNRA), Toulouse, France http://www.toulouse.inra.fr/prodom/egi-bin/ReqProdomII.pl?id_dom=PD000009&prodom_release=2000.1. Thus, the 93870 proteins of the invention include the following structural features that demonstrate their inclusion in the G-protein coupled receptor family: (1) an N-terminal extracellular domain; (2) seven transmembrane domains; (3) three extracellular loops; (4) three cytoplasmic loops, one of which includes the conserved arginine-aromatic doublet; and (5) a C-terminal cytoplasmic domain.

Please replace paragraph [0044] with the following paragraph:

[0044] The 93870 polypeptide of the invention contains a portion of the receptor coupled G-protein domain representing 76% of the receptor coupled G-protein receptor consensus pattern described in PROSITE pattern PDOC00210 (available from the ExPASy (Expert Protein Analysis System) proteomics server of the Swiss Institute of Bioinformatics (SIB), Geneva, Switzerland <http://www.expasy.ch/egi-bin/nicedoc.pl?PD0C00210>). The receptor coupled G-protein consensus pattern of the 93870 polypeptide differs at amino acid residues 114, 118, 120 and 125 of SEQ ID NO:2, wherein a "Y" is substituted for any of the "LIVMNQGA" residues at amino acid residue 114 of SEQ ID NO:2, a "L" is substituted for any of the "GSTANC" residues at amino acid residue 118 of SEQ ID NO:2, a "T" is substituted for any of the "DENH" residues at amino acid residue 120 of SEQ ID NO:2, and a "F" is substituted for any of the "LIVM" residues at amino acid residue 125 of SEQ ID NO:2.

Please replace paragraph [0046] with the following paragraph:

[0046] General information regarding PFAM identifiers, PS prefix and PF prefix domain identification numbers can be found at Sonnhammer *et al.* (1997) *Protein* 28:405-420 and <http://www.psc.edu/general/software/packages/pfam/pfam.html> the Pfam website maintained in several locations, *e.g.* by the Sanger Institute (pfam.sanger.ac.uk/Software/Pfam/HMM_search).

Please replace paragraph [0072] with the following paragraph:

[0072] The comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm. In a preferred embodiment, the percent identity between two amino acid sequences is determined using the Needleman and

Wunsch (*J. Mol. Biol.* (48):444-453 (1970)) algorithm which has been incorporated into the GAP program in the GCG software package (available at ~~http://www.gcg.com~~ the bioinformatics page of the website maintained by Accelrys, Inc., San Diego, CA, USA), using either a Blossum 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In yet another preferred embodiment, the percent identity between two nucleotide sequences is determined using the GAP program in the GCG software package (~~available at http://www.gcg.com~~), using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. A particularly preferred set of parameters (and the one that should be used if the practitioner is uncertain about what parameters should be applied to determine if a molecule is within a sequence identity or homology limitation of the invention) are a Blossum 62 scoring matrix with a gap penalty of 12, a gap extend penalty of 4, and a frameshift gap penalty of 5.

Please replace paragraph [0074] with the following paragraph:

[0074] The nucleic acid and protein sequences described herein can be used as a "query sequence" to perform a search against public databases to, for example, identify other family members or related sequences. Such searches can be performed using the NBLAST and XBLAST programs (version 2.0) of Altschul, et al. (1990) *J. Mol. Biol.* 215:403-10. BLAST nucleotide searches can be performed with the NBLAST program, score = 100, wordlength = 12 to obtain nucleotide sequences homologous to 93870 nucleic acid molecules of the invention. BLAST protein searches can be performed with the XBLAST program, score = 50, wordlength = 3 to obtain amino acid sequences homologous to 93870 protein molecules of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et al., (1997) *Nucleic Acids Res.* 25(17):3389-3402. When utilizing BLAST and Gapped BLAST programs, the default parameters of the respective programs (e.g., XBLAST and NBLAST) can be used. ~~See~~ http://www.ncbi.nlm.nih.gov (accessible at the website maintained by National Center for Biotechnology Information, Bethesda, MD, USA).

Please replace paragraph [00195] with the following paragraph:

[00195] In another embodiment, determining the ability of the 93870 protein to bind to a target molecule can be accomplished using real-time biomolecular interaction analysis (BIA; e.g., Sjolander *et al.* (1991) *Anal. Chem.* 63:2338-2345; Szabo *et al.* (1995) *Curr. Opin. Struct.*

Biol. 5:699-705). "Surface plasmon resonance" (SPR) or "BIA" detects biospecific interactions in real time, without labeling any of the interactants (e.g., ~~BIAcore~~ BIACORE™). Changes in the mass at the binding surface (indicative of a binding event) result in alterations of the refractive index of light near the surface (the optical phenomenon of SPR), resulting in a detectable signal that can be used as an indication of real-time reactions between biological molecules.

Please replace paragraph [00280] with the following paragraph:

[00280] Pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, ~~Cremophor~~ CREMOPHOR® EL solubilizer (BASF; Florham Park Parsippany, NJ) or phosphate buffered saline (PBS). In all cases, the composition must be sterile and should be fluid to the extent that easy syringability exists. It should be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as mannitol, sorbitol, sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including an agent in the composition that delays absorption, for example, aluminum monostearate and gelatin.

Please replace paragraphs [00367]-[00368] with the following paragraphs:

[00367] Human 93870 expression was measured by ~~TaqMan®~~ TAQMAN™ quantitative PCR (Perkin Elmer Applied Biosystems) in cDNA prepared from a variety of normal and diseased (e.g., cancerous) human tissues or cell lines.

[00368] Probes were designed by PrimerExpress software (PE Biosystems) based on the sequence of the human 93870 genes. Each human 93870 gene probe was labeled using FAM (6-

carboxyfluorescein), and the β 2-microglobulin reference probe was labeled with a different fluorescent dye, VIC. The differential labeling of the target gene and internal reference gene thus enabled measurement in same well. Forward and reverse primers and the probes for both β 2-microglobulin and target gene were added to the ~~TaqMan~~[®] TAQMAN™ Universal PCR Master Mix (PE Applied Biosystems). Although the final concentration of primer and probe could vary, each was internally consistent within a given experiment. A typical experiment contained 200nM of forward and reverse primers plus 100nM probe for β -2 microglobulin and 600 nM forward and reverse primers plus 200 nM probe for the target gene. ~~TaqMan~~ TAQMAN™ matrix experiments were carried out on an ABI PRISM™ 7700 Sequence Detection System (PE Applied Biosystems). The thermal cycler conditions were as follows: hold for 2 min at 50°C and 10 min at 95°C, followed by two-step PCR for 40 cycles of 95°C for 15 sec followed by 60°C for 1 min.